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10/574,034	05/02/2007	Robert Bucki	46406-0109-01US [222641]	9154

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DRINKER BIDDLE & REATH
ATTN: INTELLECTUAL PROPERTY GROUP
ONE LOGAN SQUARE, SUITE 2000
PHILADELPHIA, PA 19103-6996

EXAMINER	
DEVI, SARVAMANGALA J N	

ART UNIT	PAPER NUMBER
1645	

NOTIFICATION DATE	DELIVERY MODE
07/23/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

DBRIPDocket@dbr.com
penelope.mongelluzzo@dbr.com

Office Action Summary	Application No.	Applicant(s)	
	10/574,034	BUCKI ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 May 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 27-47* is/are pending in the application.

4a) Of the above claim(s) *1,27-39 and 43-47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *40-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 March 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *03032008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Preliminary Amendments

1) Acknowledgment is made of Applicants' preliminary amendments filed 05/05/10, 03/27/06 and 02/24/2010.

Election

2) Acknowledgment is made of Applicants' election filed 11/19/09 in response to the restriction and species election requirement mailed 06/19/09. Applicants have elected invention III, claims 40-42, and the blood and the *in vivo* species. Because Applicants did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse. See M.P.E.P § 818.03(a).

Status of Claims

3) Claims 2-36 have been canceled via the amendment filed 03/27/06.

Claim 1 has been amended via the amendment filed 03/27/06.

New claims 27-47 have been added via the amendment filed 03/27/06.

Claim 40 has been amended via the amendment filed 02/24/2010.

Claims 1, 27-39, 43-47 have been withdrawn from consideration as being directed to a non-elected invention or species. See 37 C.F.R 1.142(b) and M.P.E.P § 821.03.

Claims 1 and 27-47 are pending.

Claims 40-42 are under examination.

Information Disclosure Statement

4) Acknowledgment is made of Applicants' information disclosure statement filed 03/03/08. The information referred to therein has been considered and a signed copy is attached to this Office Action.

Priority

5) The instant application is the national stage application filed under 35 U.S.C. 371 of PCT/US04/37763, which claims priority to the provisional application 60/519,286 filed 11/12/2003.

Sequence Listing

6) Acknowledgment is made of Applicants' raw sequence listing and CRF which have been entered on 08/19/03.

Objection(s) to Specification

7) The specification of the instant application is objected to for the following reason(s):

(a) The use of the trademarks in the instant specification has been noted. For example, see 'Sepharose' at line 29 of page 31 and line 21 of page 27. Each trademark recitation should be capitalized wherever they appear. See M.P.E.P 608.01(V) and Appendix l. Although the use of trademarks is permissible in patent applications, the propriety nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks. It is suggested that Applicants examine the whole specification and make necessary changes wherever trademark recitations appear.

(b) On page 30, line 10, the address of the American Type Culture Collection is incorrect. Effective 23 March 1998, ATCC has a new address: 10801 University Boulevard, Manassas, VA 20110-2209. Amendment to the specification is suggested to reflect this. It is suggested that Applicants examine the whole specification to make similar correction to the address, wherever it appears.

(c) Line 22 of page 31 appears to include an amino acid sequence that is longer than four amino acids in length. Yet the sequence is not identified by a specific SEQ ID number as required under 37 C.F.R 1.821 through 1.825. Any sequences recited in the instant specification, which are encompassed by the definitions for nucleotide and/or amino acid sequences as set forth in 37 C.F.R. 1.821(a)(1) and (a)(2) must comply with the requirements of 37 C.F.R 1.821 through 1.825. Note that branched sequences are specifically excluded from this definition.

APPLICANT MUST COMPLY WITH THE SEQUENCE RULES WITHIN THE SAME TIME PERIOD AS IS GIVEN FOR RESPONSE TO THIS ACTION, 37 C.F.R 1.821 - 1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 C.F.R 1.821(g).

Rejection(s) under 35 U.S.C § 112, Second Paragraph

8) The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his/her invention.

9) Claims 40-42 are rejected under 35 U.S.C § 112, second paragraph, as being indefinite, for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claim 40 is indefinite in the use of the abbreviated language 'LPS', because it is unclear what does the abbreviation 'LPS' stand for. It is suggested that Applicants use the full terminology at first occurrence with the abbreviation retained within parentheses.

(b) Claim 40 is vague and indefinite in the limitation 'conditions suitable for gelsolin binding', because it is unclear what is gelsolin binding to and what specific conditions qualify as conditions suitable for gelsolin binding. Is the recited 'gelsolin binding' non-specific gelsolin binding?

(c) Claim 41 is indefinite, because it lacks proper antecedent basis in the limitations: 'administration', 'gelsolin', 'functionally equivalent peptide fragment thereof', and 'extracellular fluid'. It is suggested that Applicants provide proper antecedent basis to these limitations by inserting the limitation --the-- before each of these limitations.

(d) Analogous rejection and criticism apply to claim 42 with regard to the limitations: 'gelsolin', 'normal aggregation', 'platelets' and 'LPS-induced generalized coagulation dysfunction'.

(e) Claim 40 is indefinite, confusing and appears to be incomplete. The claim ends with 'thereby affecting platelet function'. However, the preamble of the claim states that the claimed method is 'for restoring or maintaining normal aggregation of platelets'. Is the platelet function that is being affected by the gelsolin administration step the platelet aggregation function or any function other than aggregation?

(f) Claim 42 is indefinite and confusing in the limitation: 'the patient, who is *otherwise* subject to or susceptible to LPS-induced generalized coagulation dysfunction' [Emphasis added]. It is unclear, in terms of scope, how does this limitation differ from the limitation in the base claim 40: 'the patient is subject to or susceptible to LPS-induced generalized coagulation dysfunction'.

(g) Claims 41 and 42, which depend directly or indirectly from claim 40, are also rejected as being indefinite because of the indefiniteness or vagueness identified above in the base claim.

Rejection(s) under 35 U.S.C § 102

10) The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office Action:

> A person shall be entitled to a patent unless –
> **(b)** the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11) Claims 40-42 are rejected under 35 U.S.C. § 102(b) as being anticipated by Rosen *et al.* (WO 00/55350 A1 – Applicants' IDS) as evidenced by Janmey *et al.* (*J. Biol. Chem.* 267: 11818-11823, 1992 - Applicants' IDS) and Sheu *et al.* (*Brit. J. Hematol.* 103: 29-38, 1998 - Applicants' IDS).

Rosen *et al.* disclosed a method of treating medical conditions or infectious diseases, including Gram negative bacterial infections due to *E. coli,* such as sepsis or septic shock as well as septic shock comprising intravenous administration (i.e., administration into the blood) to a patient (i.e., a subject susceptible to LPS-induced generalized coagulation dysfunction) of a therapeutically effective amount of a polypeptide comprising *SEQ ID NO: 1065* (AAB43620), a fragment or an epitope thereof that has biological activity, i.e., functionally equivalent peptide fragment. See claim 17, section 'Infectious Disease' starting at page 403; pages 371, 372, 374, 375, 384 and 395; section 'Therapeutic/Prophylactic Administration and Composition' starting at page 336; pages 405 and 406; and pages 1051-1054. The prior art polypeptide is used to modulate blood coagulation disorders and blood platelet disorders such as thrombocytopenia and to decrease or dissolve clotting. See page 373. That thrombocytopenia is a hallmark of intravascular coagulation in a patient with Gram-negative bacterial sepsis and is due to LPS in patient's blood, which LPS enhances platelet aggregation is inherent from the teachings of Rosen *et al.* in light of what is known in the art. For instance, Sheu *et al.* taught that thrombocytopenia is a hallmark of intravascular coagulation in a patient with Gram-negative bacterial sepsis and is due to LPS in patient's blood, which LPS enhances platelet aggregation. See right column on page 29. That the polypeptide, KHVVPNEVVVQRLFQVKGRR, representing amino acids 29-

48 of the prior art SEQ ID NO: 1065 represents a biologically active gelsolin or a functionally equivalent peptide fragment of gelsolin is inherent from the teachings of Rosen *et al.* in light of what is known in the art. For example, Janmey *et al.* taught the KHVVPNEVVVQRLFQVKGRR polypeptide sequence to correspond to amino acid residues 150-169 of gelsolin. See Table 1 of Janmey *et al.* Since all human or non-human patients with *E. coli* sepsis or septic shock are susceptible to LPS-induced generalized coagulation dysfunction, Rosen's patient is expected to be susceptible to LPS-induced generalized coagulation dysfunction. The Gram negative LPS-induced condition that is treated by Rosen's method, including infections due to *E. coli* (see for example pages 404-406 of Rosen *et al.*) is the same condition that is recited as being used in the instant invention (see page 16 of Applicants' specification, for example). The QRLFQVKGRR peptide from within the above-identified gelsolin sequence, shows 100% literal identity to amino acids 160-169 of SEQ ID NO: 1 of the instant invention, and is therefore the same as Applicants' gelsolin sequence. Since the prior art gelsolin sequence is the same as the Applicants' gelsolin sequence, it necessarily possesses the same function as that of Applicants' gelsolin sequence, i.e., the capacity to affect platelet function, or the capacity to maintain or restore normal aggregation of platelets. Furthermore, the intravenous administration in the prior art method of the exogenous gelsolin sequence into the patient's blood *in vivo* necessarily increases the concentration of gelsolin therein.

Claims 40-42 are anticipated by Rosen *et al.* The reference of Janmey *et al.* or Sheu *et al.* is **not** used as a secondary reference in combination with the reference of Rosen *et al.*, but rather is used to show that every element of the claimed subject matter is disclosed by Rosen *et al.* with the unrecited limitation(s) being inherent as evidenced by the state of the art. See *In re Samour* 197 USPQ 1 (CCPA 1978).

12) Claims 40-42 are rejected under 35 U.S.C. § 102(b) as being anticipated by Rothenbach *et al.* (*J. Appl. Physiol.* 96: 25-31, January 2004, *first published 02 May 2003* – Applicants' IDS).

Instant claims get the effective filing date of 11/12/2004 since the claimed invention is neither supported nor enabled in the provisional application filed 11/12/2003.

The preamble limitation 'for restoring or maintaining normal aggregation of platelets in the blood … *in vivo*' represents the intended use of the claimed method. It is noted that the only

required step of the claimed method is administering to the blood of a patient susceptible to or subject to LPS-induced generalized coagulation dysfunction a therapeutically effective amount of gelsolin or functionally equivalent peptide fragment thereof, under any conditions suitable for unspecified gelsolin binding, thereby affecting an unspecified function of platelet. It is further noted that microvascular dysfunction occurring during inflammation in trauma or burn patients is not excluded from the scope of 'generalized coagulation dysfunction' recited in claim 40. See for example, paragraph bridging pages 6 and 7 of Applicants' specification.

Rothenbach *et al.* taught a method of intravenous infusion (i.e., in to the blood *in vivo*) of up to 7.8 mg (i.e., a therapeutically effective amount) of gelsolin to burn patients, i.e., rats (i.e., patients susceptible to LPS-generalized coagulation dysfunction), which resulted in attenuation of burn-induced pulmonary microvascular dysfunction in said patients. The burn-injured rat patients had decreased levels of plasma gelsolin before gelsolin infusion, and the intravenous infusion of exogenous gelsolin increased the plasma gelsolin level to normal plasma gelsolin levels. See title; abstract; 'Methods' on page 26; 'Results'; Figure 1; page 28; and paragraph bridging pages 29 and 30. Since the prior art product administered in to the blood of the patients susceptible to LPS-generalized coagulation dysfunction and the product administered in the instantly claimed method to a patient susceptible to LPS-generalized coagulation dysfunction is the same, i.e., gelsolin, it necessarily possesses the same function as that of Applicants' gelsolin sequence, i.e., the capacity to affect platelet function, or the capacity to maintain or restore normal aggregation of platelets. Therefore, the prior art method necessarily results in the same effects as recited in the instant claims, i.e., restoration or maintenance of normal aggregation of platelets in the blood of the patients.

Claims 40-42 are anticipated by Rothenbach *et al.*

Claim Objection(s)

13) Claim 40 is objected to for lacking a preceding article before the limitation 'functionally equivalent peptide fragment thereof' in line 5.

Remarks

14) Claims 40-42 stand rejected.

15) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. The Fax number for submission of amendments, responses and/or papers is (571) 273-8300, which receives transmissions 24 hours a day and 7 days a week.

16) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (in USA or CANADA) or 571-272-1000.

17) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Robert Mondesi, can be reached on (571) 272-0956.

/S. Devi/
Primary Examiner
AU 1645

July, 2010